cumulative incidence of transplant related-mortality and relapse was 9.9 ± 4%, 24.8 ± 5%, respectively. In multivariate analyses, advanced disease status was an adverse factor for DFS (p = 0.001) and relapse (p = 0.007). These results suggest that adult acute leukemia patients without suitable related or unrelated bone marrow donors should be considered as candidates for CBT.

15

THE IMPACT OF RESOLVED HEPATITIS B INFECTION ON ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION FOR HEMATOLOGICAL MALIGNANCIES

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Serological evidence of resolved hepatitis B (HB) infection has been associated with reactivation of hepatitis after allogeneic SCT (alloSCT), but the true impact of this finding is unknown. We hypothesized that reactivation of HB could lead to worse outcomes in patients following alloSCT.

We conducted a retrospective matched-control analysis of the outcomes of 77 patients with positive HB core antibody (HBcAb) and negative HB surface antigen (HBsAg) at the time of alloSCT. All patients had hematological malignancies (including AML, CML, lymphoma, ALL, CLL and myeloma) and were transplanted between 1998 and 2007. Control patients (with negative serology for HB and other viral hepatitides) were matched by age, diagnosis, disease risk (poor vs. good), intensity of conditioning regimen (reduced vs. myeloablative) and donor type. Poor risk was defined as not being in remission or not having chemosensitive tumor before transplant, depending on the specific disease. When possible, if multiple matches were available, a control patient with the same exact disease stage, conditioning regimen and graft source (blood or bone marrow) was selected. Three patients were dropped from the comparison because no appropriate matched control was available.

The control and study groups had similar baseline patient characteristics regarding age (median 50 and 49, respectively), poor risk (51% in both groups), sibling donor (73%), reduced intensity conditioning (42%) and diagnosis. Follow-up serological studies done after transplant documented reactivation of hepatitis B (defined as the emergence of positive HBsAg) in 8 (10%) of the initially HBcAb positive and HBsAg negative patients. Two of these patients reverted back to HBsAg negativity after a period of moderate elevation of liver enzymes and are long term survivors. The other 6 patients had persistent mild elevation of ALT and AST: 2 became long term survivors, 2 died of chronic GVHD (with liver involvement) and 2 died from progression of disease. Loss of antibody response to HBc antigen with persistent negativity of HBsAg was documented in 23 patients (30%). There were no significant differences in overall survival, relapse and non-relapse mortality and incidence of acute GVHD between HBcAb positive and control groups. In conclusion, positive HBcAb status at the time of transplant does not seem to adversely affect outcomes, despite being associated with reactivation of HB infection in at least 10% of patients after alloSCT.

Overall survival and non-relapse mortality are comparable in HepBcAb positive patients and matched controls after SCT

Outcome	HepBcAb, %	Control, %	HR (95% CI)	P
OS:				
1 yr	66	64	0.99 (0.6–1.7)	0.9
2 yr	51	55	1.1 (0.7–1.8)	0.7
NRM:				
3 mo	11	5	2.1 (0.6–6.9)	0.2
1 yr	25	17	1.5 (0.7–3.1)	0.3
2 yr	31	21	1.5 (0.7–3.1)	0.3

OS: overall survival; NRM: non-relapse mortality; HR: hazard ratio; CI: confidence interval.

16

LONG-TERM RESULTS OF A GITMO RETROSPECTIVE STUDY ON HEMATOPOIETIC STEM CELL TRANSPLANTATION (HSCT) FOR PAROXYSMAL NOCTURNAL HEMOGLOBINURIA (PNH)

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Allogeneic HSCT may cure PNH. In this study we report the results of allogeneic HSCT in 26 patients (16 males and 10 females) affected by PNH who were transplanted between July 1988 and May 2007. The median age at time of HSCT was 32 years (20–60). The median time from diagnosis to HSCT was 33 months (3–208). All patients had received various treatments before HSCT including steroids, immunosuppressive drugs and growth factors. Twenty-one patients were transfusion-dependent. The median number of packed red blood cells and platelet concentrates received before HSCT was 30 (4–500) and 22 (6–86) respectively. At time of HSCT, the median peripheral hematological counts were: polymorphonucleates (PMN) 2200 (20–10204) $\times 10^9$/L, hemoglobin 8.7 g/dl (4.6–11), platelets (PLT) 78 (6–355) $\times 10^9$/L. Two patients were severely pancytopenic at time of HSCT. Twenty-four patients were transplanted from HLA identical siblings and 2 from matched unrelated donors. The donor's median age was 33 years (20–59). The conditioning regimen was myeloablative for 16 patients (Busulfan and Cyclophosphamide), whereas 10 patients received a reduced intensity conditioning including Fludarabine, Cyclophosphamide, Melphalan and Total Body Irradiation. As graft-versus-host disease (GvHD) prophylaxis, 11 patients received Cyclosporine (CSA) alone and 13 were given CSA and short course Methotrexate. Two patients received T-cell depleted marrow cells. Twenty patients were given bone marrow cells (median nucleated cells 4.1 (2.5–7.5) $\times 10^8$/kg) and 6 received peripheral blood stem cells (median CD34+ cells 4.6 (2.8–7.1) $\times 10^6$/Kg). Twenty-five patients achieved primary sustained engraftment with a median time of 17 (10–38) days to reach $>0.5 \times 10^9$/L PMN and 27 (11–322) days to reach $>50 \times 10^9$/L PLT. The probability of developing grade II-IV acute GvHD and extensive chronic GvHD was 42% and 16% respectively. The transplant related mortality at 6 months was 34%. Causes of death were infection in 4 patients, acute GvHD in 1, chronic GvHD in 2, multi-organ failure in 1 and EBV lymphoproliferative disease in 1. As of October 2007, 16 patients are alive with complete hematological recovery and no evidence of PNH at a median follow-up of 107 months (6–210). The 10-year Kaplan-Meier probability of disease-free survival is 62%. No patient developed thromboembolic disease following HSCT. This study confirms that HSCT is a curative treatment for the majority of patients with PNH.

17

PRE-TRANSPLANT INFUSION OF NATURALLY OCCURRING DONOR CD4+ CD25+ T CELLS SUPPORTS DONOR CHIMERISM IN MHC-MATCHED ALLOGENEIC HCT

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Resistance to MHC matched allogeneic hematopoietic stem cell transplant (HCT) is mediated by host T cells and remains a major complication to successful donor HCT engraftment under reduced intensity conditioning. We examined the ability of unmanipulated donor $CD4^+$ $CD25^+$ regulatory T cells (Tregs) to support donor HCT engraftment to test the hypothesis that Treg suppression of host effector $CD8^+$ T anti-donor responses would enhance donor HCT engraftment. Mice disparate for multiple minor HA were utilized for these studies: C57BL/6 ($H\text{-}2^b$, $Ly9.1^-$) mice conditioned (5.5 Gy TBI) 24 hrs earlier, were transplanted with Tregs and TCD-BM from 129P3/J ($H\text{-}2^b$, $Ly9.1^+$) mice. By four weeks post-HCT, the mean frequency of circulating donor-derived (total $Ly9.1^+$) cells was significantly higher in recipients of 4×10^6